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EXAMINER	
HANLEY, SUSAN MARIE	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,865	SIPPONEN ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 October 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/19/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claim Objections

Claims 1 and 8 are objected to because of the following informalities: The claims contain dashes which appear to emphasize limitations for the claimed method and kit. It is suggested that the dashes be changed to lower case letters followed by a closed parenthesis [i.e. a), b), etc.] to point out the limitation. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected because the phrase "method of determination of a disaccharidase enzyme" is vague. It is unclear what characteristic is being determined. That is, is it simply the presence of the enzyme or something more specific?

Claim 1 is rejected because the phrase "as such" is vague and indefinite. It is unclear how the phrase modifies or limits the nature of the biopsy sample.

Claims 1 and 8 are rejected because the term "desired" is vague. It is not clear what characteristics are being considered to make something desired.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the

explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 6 recites the broad recitation "a reagent strip", and the claim also recites "preferably a dip-and-read reagent strip" which is the narrower statement of the range/limitation.

Claim 9 is rejected because the phrase "a glucose or galactose enzyme" is vague. The claim fails to set forth the criterion to determine what type of enzyme processing is required.

Claims 8 and 10 are rejected because the word "medium" is vague and indefinite. The metes and bounds of the term are unclear.

In claim 11, "substrate " lacks antecedent basis in claim 10. Claim 10 is drawn to a "substrate medium" which may or may not be the same as a "substrate." Also, the phrase "other components" lacks antecedent basis in claim 10.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 8 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Jos et al. (1967) in light of Webster's Dictionary (1984).

Claims 1-4 are drawn to a method of determining disaccharidase activity in a biopsy sample as such taken from an individual. The phrase "as such" was held to be vague and indefinite (vide supra). Hence, the term will be interpreted in its broadest reasonable meaning, which is that the biopsy sample is in any state. For the instant rejection, the claim is interpreted to mean that the biopsy sample is intact. Claim 8 is drawn to a kit comprising a medium containing a disaccharide and a means to detect monosaccharides.

Jos et al. disclose the detection of disaccharidase activity by biopsies of intestinal tissue by a staining method. Intestinal tissue, including that of the duodenum (p. 517, Fig. 1) was fixed, intact, onto a coverslip. A solution of glucose oxidase was deposited on the fixed tissue samples and covered by a piece of thin filter paper to prevent diffusion of glucose generated by the enzymatic activity. The filter paper was moistened with chromagenic reagent and a solution containing the chromogenic reagent and substrate (lactose, maltose, trehalose or palatinose (p. 517, left column, top) was contacted with the sample through the filter paper. Tissue areas having enzymatic activity for the particular substrate were stained (p. 517, left column).

The disclosure of Jos et al. falls within the scope of claims 8. According to Webster's II Dictionary, a kit may be defined as: 1. a set of articles used for a particular purpose; 2. a set of parts or materials to be assembled; 3. a packaged set of related materials; or 4. a container for a kit (p. 667). The two separate solutions (glucose oxidase and that having substrate and

chromagen) for use in the assay disclosed by Jos et al. meet the limitations of the claim because the claimed reagents are assembled for use together to conduct the assay. The disclosure by Webster's Dictionary is a supporting reference and properly used in a rejection under of U.S.C. 102 since it describes the definition of a kit. MPEP 2131.01. Therefore, Jos et al. anticipate claims 1-4 and 8.

Claims 8-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Tyhach (EP 0072450).

Tyhach discloses a dip-and-read test device for the detection of lactase activity which is made by impregnating a strip of filter paper with a solution comprising lactose, peroxidase, glucose oxidase and other excipients. The impregnated paper was dried and a then coated with second solution of the chromagen 3,3',5,5'-tetramethylbenzidine. The broadest reasonable interpretation of "kept separately" is that the components are not intermixed or co-mingled. The two step procedure disclosed by Tyhach produces a layered strip wherein the chromogenic substance is in a separate layer on top of the other reagents. Hence, claims 8-11 are anticipated by Tyhach.

Claims 8-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Fox et al. (1991) in light of Webster's Dictionary.

Fox et al. disclose a kit for detecting disaccharides comprising two containers with reagent. Reagent A is comprised of solution containing substrate (lactose; see p.95, first paragraph, left column), glucose oxidase and peroxidase. Reagent B comprises a solution of *o*-

dianisidine (chromagen; see p. 94, right column, first full paragraph). The disclosure of Fox et al. falls within the scope of the instant claims. According to Webster's II Dictionary, a kit may be defined as: 1. a set of articles used for a particular purpose; 2. a set of parts or materials to be assembled; 3. a packaged set of related materials; or 4. a container for a kit (p. 667). The three separate solutions for use in the assay disclosed by Fox et al. meet the claims because the claimed reagents are assembled for use together and the chromagen is kept separately from the other reagents. The disclosure by Webster's Dictionary is a supporting reference and properly used in a rejection under of U.S.C. 102 since it describes the definition of a kit. MPEP 2131.01. In conclusion, Fox et al. anticipate claims 8-11.

Claims 1-5 and 7-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Smith et al. (1989) in light of Dahlqvist (1964) and Webster's Dictionary (1984).

Claims 1-5 and 7 are drawn to a method of determining disaccharidase activity in a biopsy sample as such taken from an individual. The phrase "as such" was held to be vague and indefinite (vide supra). Hence, the term will be interpreted in its broadest reasonable meaning, which is that the biopsy sample is in any state. For the instant rejection, the claim is interpreted to mean that the biopsy sample is homogenized. The remaining claims are drawn to a kit comprising a medium containing a disaccharide and a means to detect monosaccharides.

Smith et al. disclose a comparison of methods of determining lactase, sucrase and maltase activates in endoscopic biopsies from the duodenum and those in Crosby capsule biopsies from the proximal jejunum. Endoscopic duodenal biopsy samples from human patients were homogenized. Juice was aspirated from the jejunal biopsy sample. Dissacharidase activities were

measured from both types of samples adding the substrate (sucrose, maltose or lactose) to the homogenized biopsy sample. After incubation, a glucose oxidase reagent was added to the homogenate and determining the amount of glucose spectrophotometrically according to the method of Dahlqvist (p. 318, Methods).

Dahlqvist teaches that the glucose oxidase reagent comprises o-dianisidine, glucose oxidase and peroxidase (p. 20, middle of second paragraph). The disclosure of Dahlqvist is a supporting reference and properly used in a rejection under of U.S.C. 102 since it describes the method of Dahlqvist used by Smith et al. MPEP 2131.01.

Further, Smith et al., in light of Dahlqvist, teach a kit for detecting disaccharides because glucose oxidase reagent described by Dahlqvist is assembled for use together with the separate containers containing the glucose oxidase, peroxidase and chromagen. This disclosure falls within the scope of the instant claims because Webster's II Dictionary, a kit may be defined as: 1. a set of articles used for a particular purpose; 2. a set of parts or materials to be assembled; 3. a packaged set of related materials; or 4. a container for a kit (p. 667). The test strip and disaccharide substrate solutions used in the assay disclosed by Smith et al. meet the claims because the claimed reagents are assembled for use together and the chromagen is kept separately from the other reagents until it is combined with the remaining components of the glucose oxidase reagent. The disclosure by Webster's Dictionary is a supporting reference and properly used in a rejection under of U.S.C. 102 since it describes the definition of a kit. MPEP 2131.01. Therefore, claims 1-5 and 7-11 are anticipated by Smith et al. in light of Dahlqvist.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (1989) in view of Banai et al. (1984) in further view of Lee et al. (1998) and in light of Dahlqvist (1964) and Familymeds.

Claims 1-7 are drawn to a method of determining disaccharidase activity in a biopsy sample as such taken from an individual. The phrase "as such" was held to be vague and indefinite (vide supra). For the purposes of the instant rejection, the term will be interpreted by the meaning ascribed to it in the instant specification. That is, the sample is unprocessed or unhomogenized.

The disclosure of Smith et al. is discussed vide supra. Smith et al do not disclose the determination of disaccharidase activity from an unprocessed, unhomogenized endoscopic sample taken from the duodenum of an individual. Smith et al. also do not disclose the detection of disaccharidases with a reagent strip.

Banai et al. disclose a method for demonstrating disaccharidase activities in biopsy specimens obtained endoscopically from the jejunum. The biopsy samples are unprocessed and placed in a solution containing lactose or sucrose. The samples were incubated and the presence of glucose was determined with Hema-Combistix test strip from Ames (p. 185, left column). The

change in color of the strips indicated the presence of sucrase or lactase in the biopsy sample. Banai et al. conclude that this method is advantageous because it enables the endoscopist to give correct information on jejunal functions immediately after the exam (p. 185, last paragraph). The Familymeds website lists the active ingredients impregnated on the Hema-Combistix test strip are the chromagen, 3,3',5,5'-tetramethylbenzidine, glucose oxidase and Horseradish peroxidase. The disclosure by the Familymeds website is a supporting reference and serves to describe, in greater detail, the contents of the test strip used by Banai et al.

Lee et al. disclose that there is less variation in the results of the measurement of sucrase activity in intact mouse intestines when compared to mouse intestines that have been homogenized. Lee et al. teach a sucrase assay for an intact preparation of mouse small intestine by everting the sample and putting it on a sleeve which is placed in Ringer's solution, under physiological conditions. The everted sample was then incubated in a Ringer's solution containing sucrose. At the end of the incubation, the sleeve was removed and to the incubation solution was added a solution comprising glucose oxidase, horse radish peroxidase and p-hydrobenzoic acid. After incubation, the sucrase activity was determined by measuring the absorbance of the chromagen on a spectrophotomer (p. 2112, left column, fourth paragraph).

Lee et al. report that under conditions of identical pH and solution composition, the sleeve and homogenate methods yield statistically indistinguishable results (p. 2115, end of first paragraph, right column). Lee et al. note that the coefficient of variability is slightly higher for the homogenate assays. Lee et al conclude that this observation was not surprising since homogenization introduces an additional source of variability into the assay, as compared to the sucrase assay with intact mouse intestines (p. 2115, right column, third paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to determination of disaccharidase activity using an intact biopsy sample of duodenal tissue in the method disclosed by Smith et al. Both Banai et al. and Lee et al. disclose that one can successfully measure disaccharidase activities in intact biopsy specimens obtained endoscopically from the jejunum and intestines, respectively. Given that the duodenum is adjacent to the jejunum, the ordinary artisan would have had a reasonable expectation of success that disaccharidase activity could be detected from an intact biopsy sample of duodenum. The ordinary artisan would have been motivated to use intact duodenal biopsy sample in the method disclosed by Smith et al. because the elimination of the homogenization step allows the ordinary artisan to obtain correct information on duodenal functions immediately after an exam. The ordinary artisan would be further motivated to eliminate the homogenization process because homogenization introduces more variability in the assay results.

Regarding the use of a reagent strip to measure disaccharidase activity, the ordinary artisan would have been motivated to employ a reagent strip because it is more convenient than using solutions of the reagents. This convenience allows the practitioner to obtain results at the bedside of the patient. The ordinary artisan would have had a reasonable expectation that the reagent strip would correctly detect disaccharidase activity in duodenal tissue. Smith et al. demonstrated that duodenal biopsy is a valid alternative to jejunal biopsy for the determination of disaccharidase activity. Therefore, claims 1-7 are held obvious over Smith et al. in view of Banai et al. in further view of Lee et al. and in light of Dahlqvist and Familymeds.

The following reference is cited as of interest:

Ngo et al. "A Sensitive and Versiitile Chromagenic Assay for Peroxidase and Peroxidase-Coupled Reactions" Anal. Biochem. (1980) 105(2): 389-397.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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PRIMARY EXAMINER